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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SWARTZ, RODNEY P	
ART UNIT	**PAPER NUMBER**
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	05/01/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 05/01/2007.

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mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/723,908	ANDERSEN ET AL.	
	Examiner	Art Unit	
	Rodney P. Swartz, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5February2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *28-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-45* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26November2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/615,947.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' Response to Restriction Requirement, received 5 February 2007, is acknowledged. Applicants elect, with traverse, Invention I, claims 1-27, drawn to polypeptides, classified in class 424, subclass 248.1.

Applicant's election with traverse is on the grounds that Inventions I and IV could be easily examined together as being directed to DNA, polypeptides encoded by the DNA, vectors and transformed hosts. This is not found persuasive because of the reasons put forth in the original requirement, i.e., the inventions are drawn to structurally and functionally distinct molecules, and while the searches for the inventions may overlap, they are not coextensive. Therefore, the requirement is still deemed proper and is made FINAL.

Claims 1-45 are pending. Claims 28-45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

2. Claims 1-27 are under consideration.

Specification

3. The disclosure is objected to because of the following informalities:

Page 1, line 1, the priority statement should be updated to indicate that 09/615,947 is now abandoned.

Page 6, lines 5 and 8, contain an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Page 30, line 35, what is meant by "pres??ent"?

Page 34, line 1, "**FIGURE LEGENDS**" should be "Brief Description of the Drawings". See MPEP § 608.01(f).

Page 34, lines 11-17, there is no Brief Description labeled 2A, 2B, or 2C

Appropriate correction is required.

Drawings

4. Figure 1 is objected to because the Brief Description lists A, B, and C, but the figure lists 1a, 1b, and 1c.

5. Figure 2 is objected to because the Brief Description does not list 2a, 2b, and 2c. It is recommended that the figures be listed as 2A, 2B, and 2C for consistency.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Sequence Requirement

6. M.P.E.P.§2422.03, paragraph 9 recites:

> 37 CFR 1.821(d) requires the use of the assigned sequence identifier in all instances where the description or claims of a patent application discuss

sequences regardless of whether a given sequence is also embedded in the text of the description or claims of an application. This requirement is also intended to permit references, in both the description and claims, to sequences set forth in the "Sequence Listing" by the use of assigned sequence identifiers without repeating the sequence in the text of the description or claims. Sequence identifiers can also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO:23" is permissible and the fragment need not be separately presented in the"Sequence Listing." Where a sequence is embedded in the text of an application, it must be presented in a manner that complies with the requirements of the sequence rules.

Pages 37 and 38 contain sequences without the required sequence identifiers.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claim 13 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 13 provides for the use of a polypeptide, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

11. Claims 1-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, and 3 recite that the claimed fragment is "immunologically equivalent" to a polypeptide fragment encoded by a member of the *esat-6* gene family. Page 13 of the specification states that to polypeptide fragments are "immunologically equivalent" if they both satisfy property i, ii, iii, iv, v, vi, vii, **or** viii, wherein the properties are explained on page s 8-9. However, because of the word **or** in the list, there is no requirement that the two fragments actually satisfy the same property. Thus, it is unclear in the claims if "immunologically equivalent" means that the fragments exhibit the same activity, or if they can exhibit totally different activities.

Claims 4-27 depend from the claims, but do not clarify the issue.

12. Claims 1-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a substantially pure polypeptide **fragment** which has a sequence identity to a polypeptide **fragment** encoded by a member of the *esat-6* gene family. The proviso at the end of the claim recites that the substantially pure **polypeptide** is not selected from a group listing.

Claim 14, 16, 21, 25, and 27 recite a composition comprising a "polypeptide" of claim 1. It is unclear what is being claimed, i.e., a fragment, or a whole polypeptide.

Claims 2-13, 15, 17-20, 22-24, and 26 depend from these claims, but do not clarify the issue.

13. Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is drawn to a fragment "derived" from a bacterium. The specification does not define the metes and bounds of such a "derivation". Therefore, it is unclear what is meant by this term.

14. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what are the metes and bounds of "the proline rich complex" because the specification does not define the phrase. It is unclear if the term "19 kDa lipoprotein" is directed to a particular moiety or if the term encompasses and/all lipoproteins which have a molecular weight of 19 kDa.

15. Claim 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 depends from claim 17 which depends from claims 14-16. Claim 16 depends from claim 15 which depends from claim 14. Claim 14 and 15 are drawn to a composition

comprising "a" polypeptide. However, claims 16-18 appear to improperly depend from these claims because they recite multiple polypeptides bound to a polymer.

16. Claim 2-4 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 3 recite that the polypeptide fragment comprises a sequence "as shown in" SEQ ID NO:X. It is unclear what are the metes and bounds of this phrase. Does it mean that the sequence is the entire SEQ ID NO: or any subsequence of the SEQ ID NO:. Claims 4 and 9 are dependent claims, but do not clarify the indefiniteness.

17. Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what patentable structure/function is imparted upon the claim by the recitation that the composition is "in the form of" a vaccine.

18. Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what patentable structure/function is imparted upon the claim by the recitation that the composition is "in the form of" a skin test reagent.

19. Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what patentable structure/function is imparted upon the claim by the recitation that the composition is "optionally in combination" with a means for detection.

20. Claim 19 are 21-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *Mycobacterium* polypeptide fragments which induce *in vitro* cell proliferation or cytokine production from PBMCs, does not reasonably provide enablement for vaccines. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention – vaccine compositions comprising substantially pure polypeptide fragments from *Mycobacterium*.

The state of the prior art - The history of vaccination in humans against *Mycobacterium tuberculosis* disease is notorious for a lack of successful protection. In addition, at the time of filing of the instant specification, there remained a lack of correlation of success in animal models with successful vaccination of humans against mycobacterial disease, as evidenced by the review article, "Evaluation of the Protective Potency of New Tuberculosis Vaccines", Review

of Infectious Diseases, Vol. 11, Supplement 2, pages S484-S490, March-April 1989. Thus, there is a lack of predictability in the art that subunit vaccines work in humans.

The amount of direction/guidance/working examples present in the instant specification is insufficient to support the broad scope of the instant claims, i.e., a vaccine. The specification provides no examples of vaccines.

The quantity of experimentation necessary to provide sufficient support for the instant claims constitute merely an invitation to experiment without a reasonable expectation of success considering the absence of vaccines against *Mycobacterium tuberculosis* in humans.

Claim Rejections - 35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

22. Claims 1-7, 12, 14, 19, 20 and 27 rejected under 35 U.S.C. 102(e) as being anticipated by Alderson et al (U.S. Pat. No. 6,555,653, filed 5 May 1998).

The claims are drawn to a substantially pure polypeptide comprising an amino acid sequence with $\geq$70% identical to a member of the *esat-6 gene* family. One of the polypeptide reference sequences is SEQ ID NO:19. Recitations of intended use carry no patentable weight.

Alderson et al teach a clone amino acid sequence (clone mTCC#1; SEQ ID NO:143) which is 93.2% identical to instant SEQ ID NO:19.

Conclusion

23. No claims are allowed.

24. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rodney P. Swartz, Ph.D., Art Unit 1645, whose telephone number is (571) 272-0865. The examiner can normally be reached on Monday through Thursday from 9:00 AM to 7:30 PM EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Jeffrey Siew, can be reached on (571)272-0787.

The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER
Art Unit 1645

April 24, 2007